EDITORIAL COMMENT

Botulinum Toxin Type A as a Prophylactic Treatment for Chronic Daily Headache: Time to Conduct a Large Clinical Trial in Taiwan?

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Chronic daily headache (CDH) refers to a group of headache disorders that occur on at least 15 days per month.[1] It is frequently associated with the overuse of pain medications and comorbid psychiatric conditions such as anxiety and depression. Although CDH is not life-threatening, it often causes considerable disability and compromises the quality of life of those who suffer from it. Therefore, the management of CDH is a challenge for many clinicians.[2]

One of the most common subtypes of CDH is transformed migraine (TM), also known as chronic migraine (CM). Patients with TM usually have a history of episodic migraine which over the years gradually increases in frequency to become CDH, but decrease in the severity of migraine features.[1] In TM, acute migraine attacks are treated as migraine, but their prevention is difficult.[3] Conventional preventive treatments for TM include the use of β-blockers, tricyclic antidepressants, and anticonvulsants, but the results are less than satisfactory.[2] The systemic side effects of these medications also limit their usefulness as prophylactic treatments. To date, there are no randomized controlled trials of preventive therapy aimed exclusively at TM.

In the past 10 years, botulinum toxin A (BoNT-A) has emerged as a treatment for headaches, and it has been found to be safe and well tolerated in general.[4] Several open-label studies of BoNT-A treatment with small numbers of patients have reported that it is beneficial for CDH. In this issue, Liu et al[5] retrospectively analyzed the efficacy of BoNT-A in 30 consecutive patients with TM. After a single injection of a low dose of BoNT-A, 27 of the 30 patients reported at least a 50% reduction in either the number of headache days or in headache intensity. The authors concluded that BoNT-A is a promising prophylactic treatment for TM for patients in Taiwan.

On the other hand, 3 randomized, double-blind, placebo-controlled studies of BoNT-A for the treatment of CDH found negative results for their primary efficacy endpoint measured by the change from baseline in the frequency of headache-free days.[6–8] All 3 studies included patients with TM, but did not separately examine the efficacy of BoNT-A for those patients. Subgroup analysis of the study by Mathew et al[8] showed a significant reduction in the frequency of headaches in CDH patients who were not using other prophylactic medications.[9]

The mixed findings of the efficacy of BoNT-A in CDH prophylaxis shows the need to identify those patients who may benefit from BoNT-A. The report by Liu et al[5] indicates that it is likely that patients with TM may represent a subgroup of migrainers who respond better to BoNT-A, but further studies are needed. This issue is important in clinical practice because BoNT-A is costly and at the present time its use for headache prevention is not reimbursed by the National Health Insurance of Taiwan.

In the past decade, the epidemiology of headache and its subtypes has been extensively studied. Wang[10] reported that the prevalence rates of CDH in Taiwan (3.2–3.9%) were similar to those in Western countries (3.0–4.7%). However, the inclination to seek medical attention and the response to BoNT-A treatment might be different between the 2 groups. Perhaps it is

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time to conduct a well-designed, large, multicenter, randomized, double-blind, placebo-controlled study of BoNT-A for the prevention of CDH in Taiwan.

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